

PREGNANCY AND DELIVERY CHANGE THE GENE EXPRESSION OF SYNAPTIC AND EXTRASYNAPTIC GABA_A RECEPTORS IN THE RAT HIPPOCAMPUS

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In previous studies we have shown [1] that the of gene expression of selective GABA receptor subunits ($\alpha_{1,3,5}$; γ_2) during pregnancy and after delivery is functionally related to fluctuations of endogenous brain concentrations of allopregnanolone, a potent and efficacious modulator of GABA receptor. We have now studied the amount of the GABA_A receptor δ and α_4 protein during pregnancy (15, 19, 21, day) and after delivery (2 and 7 day) in rat hippocampal slices by immunohistochemistry. The GABA_A receptors containing δ and α_4 subunits largely localized at the extrasynaptic sites, are responsible for the tonic currents, and possess an enhanced sensitivity to allopregnanolone. Moreover, we also studied the amounts of α_1 , α_2 , and γ_2 which are localized in the synaptic site and are responsible for the phasic inhibition.

We found a progressive increase in the levels of the δ subunit during pregnancy with a massimal value between 19-21 days. The level of this subunit significantly decreased at days 2 and 7 after delivery. On the contrary we observed an increase in the levels of the α_4 subunit 2 days after delivery and this effect lasted for at least 7 days. However, no significant changes were observed for this subunit during pregnancy. In addition, the levels of the α_1 , α_2 , and γ_2 protein were significantly decreased and increased during pregnancy and after delivery, respectively.

Subchronic administration of finasteride, a 5 α -reductase inhibitor able to reduce the concentration of allopregnanolone more in the brain than in plasma [1], blocked the changes in the amount of δ and γ_2 proteins observed during pregnancy. In contrast, the subchronic administration of clomifene a compound that blocks estrogen action, didn't abolish the changes in the same GABA_A receptor subunits observed during pregnancy.

This study shows a marked alterations of GABA_A receptor plasticity localized at extrasynaptic and synaptic level induced by pregnancy and in the post-partum period. Changes in the expression of these receptors might be associate to affective disorders often present during pregnancy and after delivery.

[1] A. Concas et al., PNAS, 95: 13284-13289, 1998